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 Last logoff: 23apr06 08:59:56
 Logon file001 26apr06 19:36:09
***** ANNOUNCEMENTS *****

NEW FILES RELEASED

*****Regulatory Affairs Journals (File 183)**
*****Index Chemicus (File 302)**
*****Inspec (File 202)**

RELOADS COMPLETED

*****File 516, D&B--Dun's Market Identifiers**
*****File 523, D&B European Dun's Market Identifiers**
*****File 531, American Business Directory**
***** MEDLINE has been reloaded with the 2006 MeSH (Files 154 & 155)**
***** The 2005 reload of the CLAIMS files (Files 340, 341, 942)**
 is now available online.

Chemical Structure Searching now available in Prous Science Drug Data Report (F452), Prous Science Drugs of the Future (F453), IMS R&D Focus (F445/955), Pharmaprojects (F128/928), Beilstein Facts (F390), Derwent Chemistry Resource (F355) and Index Chemicus (File 302).

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>>>http://www.dialog.com/whatsnew/. You can find news about<<<

>>>a specific database by entering HELP NEWS <file number>.<<<

*** * ***

File 1:ERIC 1966-2006/Mar (c) format only 2006 Dialog

Set Items Description

--- -----

Cost is in DialUnits

?

B 155, 159, 10, 203, 35, 5, 467, 73, 434, 34

26apr06 19:36:46 User290558 Session D36.1

\$0.81 0.230 DialUnits File1

\$0.81 Estimated cost File1

\$0.16 INTERNET

\$0.97 Estimated cost this search

\$0.97 Estimated total session cost 0.230 DialUnits

SYSTEM:OS - DIALOG OneSearch

File 155:MEDLINE(R) 1951-2006/Apr 27

(c) format only 2006 Dialog

File 159:Cancerlit 1975-2002/Oct

(c) format only 2002 Dialog

***File 159: Cancerlit is no longer updating.**

Please see HELP NEWS159.

File 10:AGRICOLA 70-2006/Mar

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File 203:AGRIS 1974-2006/Nov

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File 35:Dissertation Abs Online 1861-2006/Mar

(c) 2006 ProQuest Info&Learning

File 5:Biosis Previews(R) 1969-2006/Apr W4

(c) 2006 BIOSIS

File 467:ExtraMED(tm) 2000/Dec

(c) 2001 Informania Ltd.

***File 467: F467 will close on February 1, 2006.**

7.

File 73:EMBASE 1974-2006/Apr 26

(c) 2006 Elsevier Science B.V.

File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec

(c) 1998 Inst for Sci Info

File 34:SciSearch(R) Cited Ref Sci 1990-2006/Apr W3

(c) 2006 Inst for Sci Info

Set	Items	Description
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?

S (CD 44 OR CD44) AND (L178) OR (BU75) OR (H460-16-2)

17 CD 44

24567 CD44

34 L178

5 BU75

0 H460-16-2

S1 23 (CD 44 OR CD44) AND (L178) OR (BU75) OR (H460-16-2)

?

RD S1

S2 7 RD S1 (unique items)

?

T S2/MEDIUM,K/1-7

2/K/1 (Item 1 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

(c) format only 2006 Dialog. All rts. reserv.

12817846 PMID: 10939719

A unique monoclonal antibody mNI-11 rapidly enhances spread formation in human umbilical vein endothelial cells.

Ikewaki N; Tamauchi H; Yamada A; Mori N; Yamao H; Inoue H; Inoko H

Division of Immunology, Kyushu University of Health and Welfare, Faculty of Health and Science, Nobeoka-city, Japan.

Journal of clinical immunology (UNITED STATES) Jul 2000, 20 (4) p317-24, ISSN 0271-9142--Print Journal Code: 8102137

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

... associated antigens such as mNI-58A (anti-CD11a), L130 (anti-CD18), L133.1 (anti-CD31), L178 (anti-CD44), L25.3 (anti-CD49d), or LB-2 (anti-CD54) did not carry such activity under...

2/K/2 (Item 2 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

(c) format only 2006 Dialog. All rts. reserv.

12445078 PMID: 10484683

CD3-mediated T cell activation is inhibited by anti-CD44 monoclonal antibodies directed to the hyaluronan-binding region.

Sugiyama K; Komada Y; Deguchi T; Zhang X L; Azuma E; Ido M; Yamamoto H; Sakurai M

Department of Pediatrics, Mie University School of Medicine, Tsu, Japan.

Immunological investigations (UNITED STATES) Mar-May 1999, 28 (2-3) p185-200, ISSN 0882-0139--Print Journal Code: 8504629

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

CD3-mediated T cell activation is inhibited by anti-CD44 monoclonal

antibodies directed to the hyaluronan-binding region.

The CD44 molecule has been shown to play a role in T cell adhesion and activation. We have investigated the ability of five anti- CD44 monoclonal antibodies (MoAb) including 15C6, 18A3, BU75 (Ancell), J173 (Immunotech), and L178 (Becton Dickinson) to regulate T cell activation. Three MoAb: 15C6, BU75, and J173 were found to selectively inhibit DNA synthesis, interleukin-2 (IL-2) receptor expression...

... of the cell cycle in T cells stimulated with anti-CD3 MoAb. None of anti- CD44 MoAb had influence on T cell proliferation induced by IL-2 or phorbol 12-myristate 13-acetate plus ionomycin. Inhibition of the CD3 pathway by anti- CD44 MoAb occurred by binding of MoAb directly to T cells without the involvement of monocytes or Fc receptors. In addition, the inhibitory anti- CD44 MoAb clearly suppressed intracellular calcium mobilization in T cells stimulated with anti-CD3 MoAb. Interestingly, the ability of anti- CD44 MoAb to inhibit T cell activation was well correlated with their capability to block the binding of hyaluronan (HA) to CD44 molecules. These results suggest that anti- CD44 MoAb directed to HA-binding site could selectively inhibit CD3-mediated T cell activation. Furthermore, CD44 -mediated inhibitory signals would be linked to the blocking of early CD3-mediated signal transduction.

Descriptors: *Antigens, CD3--metabolism--ME; *Antigens, CD44--metabolism--ME; *Hyaluronic Acid--metabolism--ME; *T-Lymphocytes--metabolism--ME; Animals; Antibodies, Monoclonal--biosynthesis--BI; Antibodies, Monoclonal--immunology--IM; Antigens, CD44--immunology--IM; Calcium--metabolism--ME; Cell Cycle; Humans; Intracellular Fluid--metabolism--ME; Lymphocyte Activation; Mice

Chemical Name: Antibodies, Monoclonal; Antigens, CD3; Antigens, CD44 ; Calcium; Hyaluronic Acid

2/K/3 (Item 3 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

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11808924 PMID: 9633883

Evidence for differences in the mechanisms by which antibodies against CD44 promote adhesion of erythroid and granulopoietic progenitors to marrow stromal cells.

Oostendorp R A; Spitzer E; Brandl M; Eaves C J; Dormer P

Institute for Experimental Haematology, GSF-National Research Centre for Environment and Health, Munich, Germany.

British journal of haematology (ENGLAND) Jun 1998, 101 (3) p436-45, ISSN 0007-1048--Print Journal Code: 0372544

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Evidence for differences in the mechanisms by which antibodies against CD44 promote adhesion of erythroid and granulopoietic progenitors to marrow stromal cells.

... a number of different molecules, some of which may be progenitor-lineage- and stage-specific. CD44 is one such molecule, although little is known about the mechanism(s) by which it is involved. In this study, several anti- CD44 monoclonal antibodies (mAb) increased the adherence of clonogenic cells, without affecting the total number of...

... from the adhesion cultures. All of these mAb recognized epitopes on the globular head of CD44. In contrast, two mAb that recognized other regions of CD44 reduced progenitor adhesion to stroma. The mechanism by which one of the anti- CD44 mAb (L178) enhanced progenitor adhesion did not involve CD44 -crosslinking, and was independent of VLA-4-, VLA-5- or

LFA-1-mediated interactions, Ca or Mg cations, or accessory cells. In addition, CD44 expression on both progenitors and stromal cells contributed to L178 -enhanced progenitor adhesion. Baseline adherence of erythroid progenitors to stroma required tyrosine kinase activity, whereas

...

... dependent. Taken together, the present studies indicate both similarities and differences in the mechanisms of CD44 -mediated adhesion of erythroid and granulopoietic progenitors to stromal cells.

Descriptors: *Antibodies, Monoclonal--physiology--PH; *Antigens, CD44 --immunology--IM; *Erythroid Progenitor Cells--immunology--IM; *Hematopoietic Stem Cells--immunology--IM; *Stromal Cells--immunology...

Chemical Name: Antibodies, Monoclonal; Antigens, CD44 ; Protein-Tyrosine Kinase; Adenylate Cyclase

2/K/4 (Item 4 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

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11619350 PMID: 9516861

Correlation of MYCN amplification, Trk-A and CD44 expression with clinical stage in 250 patients with neuroblastoma.

Kramer K; Cheung N K; Gerald W L; LaQuaglia M; Kushner B H; LeClerc J M; LeSauter L; Saragovi H U

Department of Pediatrics and Pathology, Memorial Sloan-Kettering Cancer Center, New York, NY 10021, USA.

European journal of cancer (Oxford, England - 1990) (ENGLAND) Oct 1997, 33 (12) p2098-100, ISSN 0959-8049--Print Journal Code: 9005373

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Correlation of MYCN amplification, Trk-A and CD44 expression with clinical stage in 250 patients with neuroblastoma.

In contrast to MYCN amplification, expression of either trk-A or CD44 in neuroblastoma is a favourable prognostic factor and were therefore investigated in tumours from 250...

... blotting or PCR amplification and was detected in 28 stage 4 tumours. Trk-A and CD44 expression was detected by immunoperoxidase staining using murine monoclonal antibodies 5C3 and L178 , respectively. Expression was scored as positive (homogeneous), mixed (heterogeneous) or non-reactive (negative). Trk-A expression was found in 95% of Group 1 tumours and 49% of Group 2 tumours. CD44 expression was found in 100% of Group 1 tumours, the majority of which had a strong homogeneous expression. Lack of CD44 expression occurred in 25% of tumours, all stage 4 neuroblastoma. Of the 28 MYCN amplified tumours, 27/28 (96%) were trk-A negative, and 13/28 (46%)

CD44 negative. We conclude that (1) a significant percentage of stage 4 neuroblastoma express either or both trk-A and CD44 , (2) the absence of CD44 expression is highly restricted to stage 4 neuroblastoma and is associated with the lack of trk-A expression, (3) trk-A negativity among CD44 -positive tumours is associated with stage 4 neuroblastoma and (4) the absence of trk-A...

Descriptors: *Antigens, CD44 --metabolism--ME; *Carrier Proteins --metabolism--ME; *Ganglioneuroma--genetics--GE; *Ganglioneuroma--metabolism--ME; *Gene Amplification; *Genes...

Chemical Name: Antigens, CD44 ; Carrier Proteins; Membrane Proteins; Neoplasm Proteins; TrkA protein; Receptor, trkA

2/K/5 (Item 5 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

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10857095 PMID: 8677750

Adhesion of human hematopoietic progenitor cells to bone-marrow-derived stromal cells is enhanced by antibodies to CD44.

Oostendorp R A; Spitzer E; Dormer P

GSF-Forschungszentrum fur Umwelt und Gesundheit, Institut fur Experimentelle Hamatologie, Munchen, Deutschland.

Acta haematologica (SWITZERLAND) 1996, 95 (3-4) p243-7, ISSN 0001-5792--Print Journal Code: 0141053

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

... human hematopoietic progenitor cells to bone-marrow-derived stromal cells is enhanced by antibodies to CD44 .

It has been suggested that CD44 mediates adhesive interactions between hematopoietic progenitor cells and the stromal microenvironment. Ligands of CD44 include several extracellular matrix components, such as hyaluronic acid and fibronectin. Antibodies against CD44 have been shown to induce homotypic T cell aggregation, and to stimulate T and natural killer cell activity. We hypothesized that CD44 could similarly amplify interactions between blast-colony-forming cells and bone marrow stromal cells (BMSCs). Indeed, we have previously found that the anti- CD44 antibody NKI-P2 enhanced VLA-4-dependent interactions. Here, we studied an additional panel of nineteen anti- CD44 antibodies from the 5th Workshop on Leukocyte Differentiation antigens, to find out whether amplification was associated with a particular CD44 epitope. None of these antibodies showed inhibitory activity, whereas nine significantly increased the number of... ..observed with epitope 1 antibodies: 4.C3 (4.4-fold), 212.3 (6.3-fold), L178 (9.1-fold), and NIH44-1 (9.2-fold). Our data suggest that primarily epitope 1 is associated with enhancement of colony formation. Furthermore, the findings support a role for CD44 as an amplifier in progenitor-BMSC interactions.

Descriptors: *Antibodies, Monoclonal--immunology--IM; *Antigens, CD44 --immunology--IM; *Bone Marrow Cells; *Cell Adhesion; *Erythroid Progenitor Cells--physiology--PH; *Stromal Cells--physiology...

Chemical Name: Antibodies, Monoclonal; Antigens, CD44 ; Epitopes; Granulocyte Colony-Stimulating Factor; Trypsin

2/K/6 (Item 1 from file: 159)

DIALOG(R)File 159:Cancerlit

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02061521 PMID: 94698328

The adhesion protein CD44 is modulated by proteolytic enzymes (Meeting abstract).

Kunze; Ransberger; Buschmans; Stauder; Gebauer

IMTOX Inc., Berlin, Germany

Non-serial 1993, Biological Response Modifiers, 2nd International Congress. January 29-31. 1993, San Diego, CA, p. 53, 1993.,

Document Type: JOURNAL ARTICLE

Languages: ENGLISH

Main Citation Owner: NOTNLM

Record type: Completed

The adhesion protein CD44 is modulated by proteolytic enzymes (Meeting abstract).

CD44 is a common membrane glycoprotein on stimulated and postnatal immunocytes. Recently, splice variants of CD44, called CD44v, were described as surface molecules on certain tumor cells. Here, the expression of...

... is correlated with the metastatic potential of the tumor cells. We investigated the sensitivity of CD44 to proteolytic cleavage by the therapeutically used proteases bromelain (B), papain (P) and trypsin (T... lymphocytes and the leukemic cell line U937 were used to study proteases-mediated modulation of CD44. The cells were treated with B, P and T (1.25-40 ug/ml, 60 min, 37 C). After direct or indirect staining with monoclonal antibodies against CD44 (L178, A3D8, J-173), we measured the altered expression of these epitopes by flow cytometry. We found a dose-dependent decrease of the detectable CD44 relative receptor density in comparison to a reference, after treatment with the thiolproteases B and ...

... a therapeutical benefit of the thiolproteases B and P in cancer treatment of tumors where CD44 is involved in the mechanisms of metastasis.

Chemical Name: Serine Proteinases; Trypsin; Papain; Bromelains; Antibodies, Monoclonal; Antigens, CD44; Carrier Proteins; Epitopes; Receptors, Cell Surface; Receptors, Lymphocyte Homing

2/K/7 (Item 1 from file: 73)

DIALOG(R)File 73:EMBASE

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12691580 EMBASE No: 2004291821

The effect of anti-CD44 monoclonal antibodies on differentiation and proliferation of human acute myeloid leukemia cells

Gadhoum Z.; Delaunay J.; Maquarre E.; Durand L.; Lancereaux V.; Qi J.; Robert-Lezenes J.; Chomienne C.; Smadja-Joffe F.

F. Smadja-Joffe, Inserm EMI 00-03, LBCH, Institut Universitaire d'Hematologie, 1 Avenue Claude Vellefaux, 75010 Paris France

AUTHOR EMAIL: fjsmadja@infobiogen.fr

Leukemia and Lymphoma (LEUK. LYMPHOMA) (United Kingdom) 2004, 45/8 (1501-1510)

CODEN: LELYE ISSN: 1042-8194

DOCUMENT TYPE: Journal ; Review

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 104

The effect of anti- CD44 monoclonal antibodies on differentiation and proliferation of human acute myeloid leukemia cells

...frequent. We have shown that specific monoclonal antibodies (mAbs, H90 and A3D8) directed to the CD44 cell surface antigen, that is strongly expressed on human AML blasts, are capable of triggering...

...blasts in AML1 to AML5 subtypes. These results have raised the perspective of developing a CD44 -targeted differentiation therapy in most AML cases. Interestingly, these anti- CD44 mAbs can also induce the differentiation of AML cell lines, inhibit their proliferation and, in... thereby contributing to decrease the size of the leukemic clone. The challenges of an anti- CD44 based differentiation therapy in AML, and its importance in relation to the new other therapies...

DRUG TERMS (UNCONTROLLED): CD44 monoclonal antibody--drug combination--cb; CD44 monoclonal antibody--drug comparison--cm; CD44 monoclonal antibody--drug development--dv; CD44 monoclonal antibody--drug interaction--it; CD44 monoclonal antibody--drug therapy--dt; CD44 monoclonal antibody--pharmacology--pd; monoclonal antibody H90--drug comparison--cm; monoclonal antibody H90--drug development... pharmacology--pd; monoclonal antibody 15C6--drug comparison--cm; monoclonal antibody 15C6--pharmacology--pd; monoclonal antibody BU75 --drug comparison--cm; monoclonal antibody BU75 --pharmacology--pd; monoclonal antibody J173--drug comparison--cm; monoclonal antibody J173 --pharmacology--pd; monoclonal antibody 8d3--drug comparison--cm; monoclonal antibody 8d3--pharmacology--pd; monoclonal antibody L178 --drug

development--dv; monoclonal antibody L178 --pharmacology--pd; monoclonal antibody S5--drug development--dv; monoclonal antibody S5--pharmacology--pd ; protein bcl...

?

Set	Items	Description
S1	23	(CD 44 OR CD44) AND (L178) OR (BU75) OR (H460-16-2)
S2	7	RD S1 (unique items)
?		

* * * * * Welcome to STN International * * * * *

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America
NEWS 2 "Ask CAS" for self-help around the clock
NEWS 3 DEC 23 New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/
 USPAT2
NEWS 4 JAN 13 IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
NEWS 5 JAN 13 New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to
 INPADOC
NEWS 6 JAN 17 Pre-1988 INPI data added to MARPAT
NEWS 7 JAN 17 IPC 8 in the WPI family of databases including WPIFV
NEWS 8 JAN 30 Saved answer limit increased
NEWS 9 FEB 21 STN AnaVist, Version 1.1, lets you share your STN AnaVist
 visualization results
NEWS 10 FEB 22 The IPC thesaurus added to additional patent databases on STN
NEWS 11 FEB 22 Updates in EPFULL; IPC 8 enhancements added
NEWS 12 FEB 27 New STN AnaVist pricing effective March 1, 2006
NEWS 13 FEB 28 MEDLINE/LMEDLINE reload improves functionality
NEWS 14 FEB 28 TOXCENTER reloaded with enhancements
NEWS 15 FEB 28 REGISTRY/ZREGISTRY enhanced with more experimental spectral
 property data
NEWS 16 MAR 01 INSPEC reloaded and enhanced
NEWS 17 MAR 03 Updates in PATDPA; addition of IPC 8 data without attributes
NEWS 18 MAR 08 X.25 communication option no longer available after June 2006
NEWS 19 MAR 22 EMBASE is now updated on a daily basis
NEWS 20 APR 03 New IPC 8 fields and IPC thesaurus added to PATDPAFULL
NEWS 21 APR 03 Bibliographic data updates resume; new IPC 8 fields and IPC
 thesaurus added in PCTFULL
NEWS 22 APR 04 STN AnaVist \$500 visualization usage credit offered
NEWS 23 APR 12 LINSPEC, learning database for INSPEC, reloaded and enhanced
NEWS 24 APR 12 Improved structure highlighting in FQHIT and QHIT display
 in MARPAT
NEWS 25 APR 12 Derwent World Patents Index to be reloaded and enhanced during
 second quarter; strategies may be affected

NEWS EXPRESS FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,
 CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
 AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.
 V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT
<http://download.cas.org/express/v8.0-Discover/>

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* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 20:24:39 ON 26 APR 2006


```
=> file caplus, bioeng, biotechno, biotechds, esbiobase
COST IN U.S. DOLLARS          SINCE FILE          TOTAL
                                ENTRY          SESSION
FULL ESTIMATED COST          0.21          0.21
```

FILE 'CAPLUS' ENTERED AT 20:25:17 ON 26 APR 2006
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```
=> s (cd44 or CD 44) and (L178) or (BU75) or (H460-16-2)
L178 NOT FOUND
The L-number entered could not be found. To see the definition
of L-numbers, enter DISPLAY HISTORY at an arrow prompt (=>).
```

```
=> s (cd44 or CD 44) and (1178) or (BU75) or (H460-16-2)
L178 NOT FOUND
The L-number entered could not be found. To see the definition
of L-numbers, enter DISPLAY HISTORY at an arrow prompt (=>).
```

```
=> s (cd44 or CD 44) and (178) or (BU75) or (H460-16-2)
L1          15 (CD44 OR CD 44) AND (178) OR (BU75) OR (H460-16-2)
```

```
=> duplicate remove L1
DUPLICATE PREFERENCE IS 'CAPLUS, BIOTECHDS, ESBIOBASE'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L1
L2          11 DUPLICATE REMOVE L1 (4 DUPLICATES REMOVED)
```

```
=> d L2 bib abs 1-11
```

L2 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

Full Text	Citing References
--------------	----------------------

```
AN 2005:409005 CAPLUS
DN 142:446013
TI Antibodies mediating cytotoxicity for cells evidencing surface expression
of CD44
IN Young, David S. f.; Hahn, Susan E.; Findlay, Helen P.
PA Can.
SO U.S. Pat. Appl. Publ., 28 pp., Cont.-in-part of U.S. Ser. No. 647,818.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 18
```

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	US 2005100542	A1	20050512	US 2004-810165	20040326
	US 6180357	B1	20010130	US 1999-415278	19991008
	CA 2456077	AA	20030912	CA 2000-2456077	20001108
	AU 2001226985	A1	20030916	AU 2001-226985	20001108
	EP 1360208	A1	20031112	EP 2000-990113	20001108
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2005519120	T2	20050630	JP 2003-573033	20001108
	US 2002041877	A1	20020411	US 2000-727361	20001129
	US 6657048	B2	20031202		
	CA 2471206	AA	20030710	CA 2001-2471206	20011221
	AU 2002226211	A1	20030715	AU 2002-226211	20011221
	EP 1455819	A1	20040915	EP 2001-995525	20011221
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2005518393	T2	20050623	JP 2003-556091	20011221
	US 2004105815	A1	20040603	US 2003-603000	20030623
	US 2005008646	A1	20050113	US 2003-647818	20030822
	WO 2005092375	A1	20051006	WO 2005-CA441	20050323
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRAI	US 1999-415278	A2	19991008		
	US 2000-727361	A2	20001129		
	US 2003-603000	A2	20030623		
	US 2003-647818	A2	20030822		
	WO 2000-IB2050	W	20001108		
	WO 2001-CA1838	W	20011221		
	US 2003-413755	A2	20030414		
	US 2004-810165	A	20040326		

AB This invention relates to the diagnosis and treatment of cancerous diseases, particularly to the mediation of cytotoxicity of tumor cells; and most particularly to the use of cancerous disease modifying antibodies (CDMAB), optionally in combination with one or more chemotherapeutic agents, as a means for initiating the cytotoxic response. The invention further relates to binding assays which utilize the CDMABs of the instant invention.

L2 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

Full Text	Citing References
-----------	-------------------

AN	2005:34440	CAPLUS
DN	142:112461	
TI	Cytotoxicity mediation of cells evidencing surface expression of CD44	
IN	Young, David S. F.; Hahn, Susan E.; Findlay, Helen P.	
PA	Can.	
SO	U.S. Pat. Appl. Publ., 37 pp., Cont.-in-part of U.S. Ser. No. 603,000. CODEN: USXXCO	
DT	Patent	
LA	English	

FAN.CNT 18

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2005008646	A1	20050113	US 2003-647818	20030822
	US 6180357	B1	20010130	US 1999-415278	19991008
	CA 2456077	AA	20030912	CA 2000-2456077	20001108
	AU 2001226985	A1	20030916	AU 2001-226985	20001108
	EP 1360208	A1	20031112	EP 2000-990113	20001108
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2005519120	T2	20050630	JP 2003-573033	20001108
	US 2002041877	A1	20020411	US 2000-727361	20001129
	US 6657048	B2	20031202		
	CA 2471206	AA	20030710	CA 2001-2471206	20011221
	AU 2002226211	A1	20030715	AU 2002-226211	20011221
	EP 1455819	A1	20040915	EP 2001-995525	20011221
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2005518393	T2	20050623	JP 2003-556091	20011221
	US 2004105815	A1	20040603	US 2003-603000	20030623
	US 2005100542	A1	20050512	US 2004-810165	20040326
	AU 2004266045	A1	20050303	AU 2004-266045	20040820
	WO 2005018667	A1	20050303	WO 2004-CA1546	20040820
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRAI	US 1999-415278	A2	19991008		
	US 2000-727361	A2	20001129		
	US 2003-603000	A2	20030623		
	WO 2000-IB2050	W	20001108		
	WO 2001-CA1838	W	20011221		
	US 2003-413755	A2	20030414		
	US 2003-647818	A2	20030822		
	WO 2004-CA1546	W	20040820		
AB	This invention relates to the diagnosis and treatment of cancerous diseases, particularly to the mediation of cytotoxicity of tumor cells; and most particularly to the use of cancerous disease modifying antibodies (CDMAB), optionally in combination with one or more chemotherapeutic agents, as a means for initiating the cytotoxic response. The invention further relates to binding assays which utilize the CDMABs of the instant invention.				
L2	ANSWER 3 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1				
	Full Text	Citing References			
AN	2004:451465 CAPLUS				
DN	141:5799				
TI	Cancerous disease modifying antibodies				
IN	Young, David S. F.; Findlay, Helen P.; Hahn, Susan E.; Takahashi, Miyoko				
PA	Can.				

SO U.S. Pat. Appl. Publ., 27 pp., Cont.-in-part of U.S. Ser. No. 413,755.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 18

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	<u>US 2004105815</u>	A1	20040603	<u>US 2003-603000</u>	20030623
	<u>US 6180357</u>	B1	20010130	<u>US 1999-415278</u>	19991008
	<u>CA 2456077</u>	AA	20030912	<u>CA 2000-2456077</u>	20001108
	<u>AU 2001226985</u>	A1	20030916	<u>AU 2001-226985</u>	20001108
	<u>EP 1360208</u>	A1	20031112	<u>EP 2000-990113</u>	20001108
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	<u>JP 2005519120</u>	T2	20050630	<u>JP 2003-573033</u>	20001108
	<u>US 2002041877</u>	A1	20020411	<u>US 2000-727361</u>	20001129
	<u>US 6657048</u>	B2	20031202		
	<u>CA 2471206</u>	AA	20030710	<u>CA 2001-2471206</u>	20011221
	<u>AU 2002226211</u>	A1	20030715	<u>AU 2002-226211</u>	20011221
	<u>EP 1455819</u>	A1	20040915	<u>EP 2001-995525</u>	20011221
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	<u>JP 2005518393</u>	T2	20050623	<u>JP 2003-556091</u>	20011221
	<u>US 6794494</u>	B1	20040921	<u>US 2003-413755</u>	20030414
	<u>US 2005008646</u>	A1	20050113	<u>US 2003-647818</u>	20030822
	<u>US 2005100542</u>	A1	20050512	<u>US 2004-810165</u>	20040326
	<u>AU 2004248865</u>	A1	20041229	<u>AU 2004-248865</u>	20040608
	<u>CA 2530214</u>	AA	20041229	<u>CA 2004-2530214</u>	20040608
	<u>WO 2004112834</u>	A1	20041229	<u>WO 2004-CA845</u>	20040608
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	<u>EP 1635869</u>	A1	20060322	<u>EP 2004-737787</u>	20040608
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
PRAI	<u>US 1999-415278</u>	A2	19991008		
	<u>US 2000-727361</u>	A2	20001129		
	<u>US 2003-413755</u>	A2	20030414		
	<u>WO 2000-IB2050</u>	W	20001108		
	<u>WO 2001-CA1838</u>	W	20011221		
	<u>US 2003-603000</u>	A2	20030623		
	<u>US 2003-647818</u>	A2	20030822		
	<u>WO 2004-CA845</u>	W	20040608		

AB The present invention relates to a method for producing patient cancerous disease modifying antibodies using a novel paradigm of screening. By segregating the anti-cancer antibodies using cancer cell cytotoxicity as an end point, the process makes possible the prodn. of anti-cancer antibodies for therapeutic and diagnostic purposes. The antibodies can be used in aid of staging and diagnosis of a cancer, and can be used to treat

primary tumors and tumor metastases. The anti-cancer antibodies can be conjugated to toxins, enzymes, radioactive compds., and hematogenous cells. The cancerous disease modifying monoclonal antibody, designated as **H460-16-2**, was produced from the hybridoma cell line clone deposited with the ATCC and designated PTA-4621.

L2 ANSWER 4 OF 11 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN

Full
Text

AN 2004-16640 BIOTECHDS

TI Treating patient suffering from cancerous disease by administering to patient individually customized anti-cancer antibodies such as 1LN-8 or 4BD-1, which are cytotoxic against cancerous cells and benign to non-cancerous cells;

cytotoxic humanized monoclonal antibody production useful for cancer therapy

AU YOUNG D S F; TAKAHASHI M

PA YOUNG D S F; TAKAHASHI M

PI US 2004101530 27 May 2004

AI US 2003-713642 13 Nov 2003

PRAI US 2003-713642 13 Nov 2003; US 1999-415278 8 Oct 1999

DT Patent

LA English

OS WPI: 2004-399654 [37]

AN 2004-16640 BIOTECHDS

AB DERWENT ABSTRACT:

NOVELTY - Treating patient suffering from cancerous disease, involves administering to patient individually customized anti-cancer antibodies or their fragments such as 1LN-8 or 4BD-1, the antibodies including subset of antibodies are cytotoxic against cancerous cells, the subset is essentially benign to non-cancerous cells, where antibodies are placed in admixture with adjuvant and are administered in amount to mediate treatment of cancerous disease.

DETAILED DESCRIPTION - Treating (M1) a patient suffering from a cancerous disease, involves administering to the patient anti-cancer antibodies or its fragments produced in accordance with a method for the production of individually customized anti-cancer antibodies which are useful in treating a cancerous disease, the antibodies including a subset of antibodies or its fragments characterized as cytotoxic against cells of a cancerous tissue, the subset is essentially benign to non-cancerous cells, where one or more antibodies or its fragments selected from the subset are placed in admixture with an adjuvant and are administered in an amount effective to mediate treatment of the cancerous disease, the one or more antibodies or its fragments are chosen from 1LN-8, 4BD-1, 4BD-3, 4BD-6, 4BD-9, 4BD-13, 4BD-18, 4BD-20, 4BD-25, 4BD-26, 4BD-27, 4BD-28, 4BD-32, 4BD-37, 4BD-50, 6BD-1, 6BD-3, 6BD-5, 6BD-11, 6BD-25, 7BD-7, 7BD-12-1, 7BD-12-2, 7BD-13, 7BD-14, 7BD-19, 7BD-21, 7BD-24, 7BD-29, 7BD-30, 7BD-31, 7BDI-17, 7BDI-58, 7BDI-60, 7BDI-62, 5LAC2, 5LAC4, 5LAC20, 5LAC23, H460-1, H460-4, H460-5, H460-10, H460-14, H460-16-1, **H460-16-2**, a H460-23 and a H460-27 monoclonal antibody or their combination. INDEPENDENT CLAIMS are also included for the following: (1) anti-cancer antibodies or their fragments chosen from 1LN-8, 4BD-1, 4BD-3, 4BD-6, 4BD-9, 4BD-13, 4BD-18, 4BD-20, 4BD-25, 4BD-26, 4BD-27, 4BD-28, 4BD-32, 4BD-37, 4BD-50, 6BD-1, 6BD-3, 6BD-5, 6BD-11, 6BD-25, 7BD-7, 7BD-12-1, 7BD-12-2, 7BD-13, 7BD-14, 7BD-19, 7BD-21, 7BD-24, 7BD-29, 7BD-30, 7BD-31, 7BDI-17, 7BDI-58, 7BDI-60, 7BDI-62, 5LAC2, 5LAC4, 5LAC20, 5LAC23, H460-1, H460-4, H460-5, H460-10, H460-14, H460-16-1, **H460-16-2**, a H460-23 and a H460-27 monoclonal antibody or their combinations; and (2) isolating or screening for cancerous cells or a

binding assay to determine presence of cancerous cells in a tissue sample chosen from tumor originating in colon, prostate, ovarian, lung, breast, skin tissue, involves providing a tissue sample from a tumor originating in colon, prostate, ovarian, lung, breast, or skin tissue, providing an isolated monoclonal antibody or its antigen binding fragment encoded by the clone deposited with the ATCC as Accession Number PTA-2700, contacting the isolated monoclonal antibody or its antigen binding fragment with the tissue sample, and determining binding of the isolated monoclonal antibody or its antigen binding fragment with the tissue sample, and thus the presence of the cancerous cells in the tissue sample is indicated and the cancerous cells are isolated by their binding.

BIOTECHNOLOGY - Preferred Method: In (M1), the one or more antibodies or its fragments chosen from subset are humanized. (M1) further involves conjugating the subset of antibodies or their fragment with a member chosen from toxins, enzymes, radioactive compounds and hematogenous cells, and administering conjugated antibodies or their fragment to the patient, where the conjugated antibodies are placed in admixture with an adjuvant and are administered in an amount effective to mediate treatment of the cancerous disease. In (M1), the cytotoxicity of the antibodies or their fragment is mediated through antibody dependent cellular toxicity, complement dependent cellular toxicity, catalyzing of the hydrolysis of cellular chemical bonds, producing an immune response against putative cancer antigens residing on tumor cells, targeting of cell membrane proteins to interfere with their function, or through production of a conformational change in a cellular protein effective to produce a signal to initiate cell-killing. The method of producing antibodies utilizes a tissue sample containing cancerous and non-cancerous cells obtained from a particular individual.

ACTIVITY - Cytostatic. No supporting data is given.

MECHANISM OF ACTION - Immunotherapy.

USE - (M1) is useful for treating a patient suffering from a cancerous disease (claimed).

ADVANTAGE - Each individual who presents with cancer is unique and has a cancer that is as different from other cancers as that person's identity. Despite this, current therapy treats all patients with the same type of cancer, at the same stage, in the same way. At least 30% of these patients will fail the first line therapy, thus leading to further rounds of treatment and the increased probability of treatment failure, metastases, and ultimately, death. By using patient specific anti-cancer antibodies, customization of cancer therapy may be possible. (23 pages)

L2 ANSWER 5 OF 11 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN

Full
Text

AN 2002-16375 BIOTECHDS
TI Individually customized anti-cancer antibodies or their fragments, useful for treating, diagnosing, prognosing and monitoring cancer;
antibody production via cell culture useful for disease therapy and diagnosis
AU YOUNG D S F; TAKAHASHI M
PA YOUNG D S F; TAKAHASHI M
PI US 2002041877 11 Apr 2002
AI US 1999-727361 8 Oct 1999
PRAI US 2000-727361 29 Nov 2000
DT Patent
LA English
OS WPI: 2002-381941 [41]
AN 2002-16375 BIOTECHDS
AB DERWENT ABSTRACT:

NOVELTY - Individually customized anti-cancer antibodies (AB1) or their fragments, are new.

DETAILED DESCRIPTION - Individually customized anti-cancer antibodies (AB1) or their fragments, are new. AB1 or their fragments are selected from: (a) 1LN-8, 4BD-1, a 4BD-3, a 4BD-6, a 4BD-9, a 4BD-13, a 4BD-18, a 4BD-20, a 4BD-25, a 4BD-26, a 4BD-27, a 4BD-28, a 4BD-32, a 4BD-37, a 4BD-50, a 6BD-1, a 6BD-3, a 6BD-5, a 6BD-11, a 6BD-25, a 7BD-7, a 7BD-12-1, a 7BD-12-2, a 7BD-13, a 7BD-14, a 7BD-19, a 7BD-21, a 7BD-24, a 7BD-29, a 7BD-30, a 7BD-31, a 7BDI-17, a 7BDI-58, a 7BDI-60, a 7BDI-62, a 5LAC2, a 5LAC4, a 5LAC20, a 5LAC23, a H460-1, a H460-4, a H460-5, a H460-10, a H460-14, a H460-16-1, a **H460-16-2**, a H460-23 or a H460-27 monoclonal antibody or their combinations; or (b) antibodies or their fragments produced by a hybridoma cell line having an ATCC Accession Number which is not defined in the specification. An INDEPENDENT CLAIM is included for methods (M1) for treating a patient suffering from a cancerous disease.

ACTIVITY - Cytostatic. No biological data given.

MECHANISM OF ACTION - The cytotoxicity of the antibodies or their fragments is mediated through antibody dependent cellular toxicity, complement dependent cellular toxicity, catalyzing of the hydrolysis of cellular chemical bonds, producing an immune response against putative cancer antigens residing on tumor cells, targeting of cell membrane proteins to interfere with their function, or through production of a conformational change in a cellular protein effective to produce a signal to initiate cell-killing (claimed). No biological data given.

USE - The patient specific antibodies are useful for treating cancer. The antibodies can also be used for diagnosis, prognosis, and monitoring of cancer.

EXAMPLE - Biopsy specimens of breast, melanoma, and lung tumors were obtained and stored at -70 degrees Centigrade until used. Single cell suspensions were prepared and fixed with -30 degrees Centigrade, 70% ethanol, washed with phosphate buffered saline (PBS) and reconstituted to an appropriate volume for injection. Balb/c mice were immunized with 2.5×10^5 (to the power of 5) - 1×10^6 (to the power of 6) cells and boosted every third week until a final pre-fusion boost was performed three days prior to the splenectomy. The hybridomas were prepared by fusing the isolated splenocytes with Sp2/0 and NS1 myeloma partners. The supernatants from the fusions were tested for subcloning of the hybridomas. Cells (including A2058 melanoma cells, CCD-12CoN fibroblasts, MCF-12A breast cells among others) were obtained from ATCC and cultured according to enclosed instructions. The HEY cell line was a gift from Dr. Inka Brockhausen. The non-cancer cells, e.g. CCD-12CoN fibroblasts and MCF-12A breast cells, were plated into 96-well microtitre plates (NUNC) 1 to 2 weeks prior to screening. The cancer cells, e.g. HEY, A2058, BT 483, and HS294t, were plated two or three days prior to screening. The plated normal cells were fixed prior to use. The plates were washed with 100 microliters of PBS for 10 minutes at room temperature and then aspirated dry. Seventy five microliters of 0.01 percent glutaraldehyde diluted in PBS were added to each well for five minutes and then aspirated. The plates were washed with 100 microliters of PBS three times at room temperature. The wells were emptied and 100 microliters of one percent human serum albumin in PBS was added to each well for one hour at room temperature. The plates were then stored at four degrees Celsius. Prior to the transfer of the supernatant from the hybridoma plates the fixed normal cells were washed three times with 100 microliters of PBS at room temperature. After aspiration to the microliters of the primary hybridoma culture supernatants were transferred to the fixed cell plates and

incubated for two hours at 37 degrees Celsius in a 8 percent carbon-dioxide incubator. The hybridoma supernatants derived from melanoma was incubated with CCD-12CoN cells and those derived from breast cancer were incubated with MCF-12a cells. After incubation the absorbed supernatant was divided into two 75 microliter portions and transferred to target cancer cell plates. Prior to the transfer the cancer cell plates were washed three times with 100 microliters of PBS. The supernatant from the CCD-12 CoN cells were transferred to the A2058 and the HS294t cells, whereas the supernatant from MCF-12A cells were transferred to the HEY and BT 483 cells. The cancer cells were incubated with the hybridoma supernatants for 18 hours at 37 degrees Celsius in an 8 percent carbon-dioxide incubator. The Live/Dead cytotoxicity assay was obtained from Molecular Probes. The assays were performed according to the manufacturer's instructions with the changes outlined below. The plates with the cells were washed once with 100 microliters of PBS at 37 degrees Centigrade, 75 to 100 microliters of supernatant from the hybridoma microtitre plates were transferred to the cell plates and incubated in a 8% carbon-dioxide incubator for 18-24 hours. Then, the wells that served as the all dead control were aspirated until empty and 50 microliters of 70% ethanol was added. The plate was then emptied by inverting and blotted dry. Room temperature PBS was dispensed into each well from a multichannel squeeze bottle, tapped three times, emptied by inversion and then blotted dry. Fifty microliters of the fluorescent Live/Deaddye diluted in PBS was added to each well and incubated at 37 degrees Centigrade in a 5% carbon-dioxide incubator for one hour. The plates were read in a Perkin-Elmer HTS7000 fluorescence plate reader and the data was analyzed in Microsoft Excel. Four rounds of screening were conducted to produce single clone hybridoma cultures. For two rounds of screening the hybridoma supernatants were tested only against the cancer cells. In the last round of screening the supernatant was tested against a number of non-cancer cells as well as the target cells indicated in the specification. The antibodies were isotyped using a commercial isotyping kit. A number of monoclonal antibodies were produced in accordance with the method of the present invention. These antibodies, whose characteristics are summarized in the specification, are identified as 3BD-3, 3BD-6, 3BD-8, 3BD-9, 3BD-15, 3BD-25, 3BD-26 and 3BD-27. Each of the designated antibodies is produced by a hybridoma cell line deposited with the American Type Culture Collection at 10801 University Boulevard, Manassas, Va. having an ATCC Accession Number which is not defined in the specification. These antibodies were considered monoclonal after four rounds of limiting dilution cloning. The anti-melanoma antibodies did not produce significant cancer cell killing. The panel of anti-breast cancer antibodies killed 32-87% of the target cells and less than 1-3% of the control cells. The predominant isotype was IgG1 even though it was expected that the majority of anti-tumor antibodies would be directed against carbohydrate antigens, and thus, be of the IgM type. There is a high therapeutic index since most antibodies spare the control cells from cell death. (13 pages)

L2 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

Full Text	Citing References
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AN 2000:240985 CAPLUS

DN 132:292701

TI Novel methods for therapeutic vaccination

IN Steinaa, Lucilla; Mouritsen, Soren; Nielsen, Klaus Gregorious; Haaning, Jesper; Leach, Dana; Dalum, Iben; Gautam, Anand; Birk, Peter; Karlsson, Gunilla

PA M & E Biotech A/S, Den.
 SO PCT Int. Appl., 220 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	<u>WO 2000020027</u>	A2	20000413	<u>WO 1999-DK525</u>	19991005
	<u>WO 2000020027</u>	A3	20001012		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	<u>CA 2345817</u>	AA	20000413	<u>CA 1999-2345817</u>	19991005
	<u>AU 9958510</u>	A1	20000426	<u>AU 1999-58510</u>	19991005
	<u>AU 751709</u>	B2	20020822		
	<u>EP 1117421</u>	A2	20010725	<u>EP 1999-945967</u>	19991005
	<u>EP 1117421</u>	B1	20040616		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, IE, SI, LT, LV, FI, RO				
	<u>TR 200100936</u>	T2	20010821	<u>TR 2001-200100936</u>	19991005
	<u>JP 2002526419</u>	T2	20020820	<u>JP 2000-573386</u>	19991005
	<u>EE 200100203</u>	A	20021015	<u>EE 2001-203</u>	19991005
	<u>NZ 511055</u>	A	20031031	<u>NZ 1999-511055</u>	19991005
	<u>AT 269100</u>	E	20040715	<u>AT 1999-945967</u>	19991005
	<u>PT 1117421</u>	T	20041130	<u>PT 1999-945967</u>	19991005
	<u>ES 2222728</u>	T3	20050201	<u>ES 1999-945967</u>	19991005
	<u>EP 1502602</u>	A2	20050202	<u>EP 2004-76709</u>	19991005
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	<u>NO 2001001586</u>	A	20010531	<u>NO 2001-1586</u>	20010328
	<u>ZA 2001002603</u>	A	20020930	<u>ZA 2001-2603</u>	20010329
	<u>US 7005498</u>	B1	20060228	<u>US 2001-806703</u>	20010430
	<u>HR 2001000319</u>	A1	20020630	<u>HR 2001-319</u>	20010504
	<u>US 2004141958</u>	A1	20040722	<u>US 2003-441779</u>	20030519
	<u>US 2006008465</u>	A1	20060112	<u>US 2005-202516</u>	20050811
PRAI	<u>DK 1998-1261</u>	A	19981005		
	<u>US 1998-105011P</u>	P	19981020		
	<u>EP 1999-945967</u>	A3	19991005		
	<u>US 1999-413186</u>	A1	19991005		
	<u>WO 1999-DK525</u>	W	19991005		
	<u>US 2001-806703</u>	A3	20010430		

AB A method is disclosed for inducing cell-mediated immunity against cellular antigens. More specifically, the invention provides for a method for inducing cytotoxic T-lymphocyte immunity against weak antigens, notably self-proteins. The method entails that antigen presenting cells are induced to present at least one CTL epitope of the weak antigen and at the same time presenting at least one foreign T-helper lymphocyte epitope. In a preferred embodiment, the antigen is a cancer specific antigen, e.g. prostate specific membrane antigen (PSM), Her2, or FGF8b. The method can be exercised by using traditional polypeptide vaccination, but also by using live attenuated vaccines or nucleic acid vaccination. The invention

furthermore provides immunogenic analogs of PSM, Her2 and FGF8b, as well as nucleic acid mols. encoding these analogs. Also vectors and transformed cells are disclosed. The invention also provides for a method for identification of immunogenic analogs of weak or non-immunogenic antigens.

L2 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2

	Full Text	Citing References
AN	2000:157009	CAPLUS
DN	133:148306	
TI	Prognostic value of the expression of E-cadherin and β -catenin in bladder cancer	
AU	Garcia del Muro, X.; Torregrosa, A.; Munoz, J.; Castellsague, X.; Condom, E.; Vignes, F.; Arance, A.; Fabra, A.; Germa, J. R.	
CS	Department of Medical Oncology, Institut Catala d'Oncologia, L'Hosp. de Llobregat, Barcelona, E-08907, Spain	
SO	European Journal of Cancer (2000), 36(3), 357-362 CODEN: EJCAEL; ISSN: 0959-8049	
PB	Elsevier Science Ltd.	
DT	Journal	
LA	English	
AB	<p>The purpose of this study was to assess the prognostic effect of the expression of E-cadherin, β-catenin and CD44 adhesion mols. in bladder carcinoma. 22 Superficial and 18 invasive bladder tumor samples were studied by immunohistochem. The median follow-up was 24 mo (range: 1-50 mo). Loss of E-cadherin and β-catenin immunoreactivity was found in 14 (35%) and 17 (43%) tumors, resp., and was significantly assocd. with invasiveness, high grade and p53 overexpression. There was no correlation between CD44 variant expression and clinicopathol. findings. Loss of E-cadherin expression was an independent predictor of poor survival in a multivariate anal., when assessed with age, grade, stage and p53 status (hazards ratio adjusted (HRa)=4.45 [95% confidence interval (CI), 1.06-18.63]). This effect was particularly augmented in patients with invasive bladder cancer. When expression of E-cadherin and β-catenin were evaluated simultaneously, loss of immunoreactivity of both proteins was a strong predictor of poor survival (HRa=13.06 [95% CI, 0.95-178.55]). The same pattern was found when progression-free survival in relation to these variables was assessed. In conclusion, assessment of E-cadherin and β-catenin immunoreactivity may be a useful prognostic marker in bladder cancer complementary to established prognostic factors.</p>	

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 3

	Full Text	Citing References
AN	1999:408455	CAPLUS
DN	131:241957	
TI	CD3-mediated T-cell activation is inhibited by anti-CD44 monoclonal antibodies directed to the hyaluronan-binding region	
AU	Sugiyama, Kenji; Komada, Yoshihiro; Deguchi, Takao; Zhang, Xiao-Li; Azuma, Eiichi; Ido, Masaru; Yamamoto, Hatsumi; Sakurai, Minoru	
CS	Department of Pediatrics, Mie University School of Medicine, Mie, 514-8507, Japan	
SO	Immunological Investigations (1999), 28(2 & 3), 185-200 CODEN: IMINEJ; ISSN: 0882-0139	

PB Marcel Dekker, Inc.

DT Journal

LA English

AB The CD44 mol. has been shown to play a role in T cell adhesion and activation. The authors have investigated the ability of 5 anti-CD44 monoclonal antibodies (MoAb) to regulate T cell activation. Three MoAb: 15C6, **BU75**, and J173 were found to selectively inhibit DNA synthesis, interleukin-2 (IL-2) receptor expression, and G1.fwdarw.S transition of the cell cycle in T cells stimulated with anti-CD3 MoAb. None of anti-CD44 MoAb had influence on T cell proliferation induced by IL-2 or phorbol 12-myristate 13-acetate plus ionomycin. Inhibition of the CD3 pathway by anti-CD44 MoAb occurred by binding of MoAb directly to T cells without the involvement of monocytes or Fc receptors. In addn., the inhibitory anti-CD44 MoAb clearly suppressed intracellular calcium mobilization in T cells stimulated with anti-CD3 MoAb. Interestingly, the ability of anti-CD44 MoAb to inhibit T cell activation was well correlated with their capability to block the binding of hyaluronan (HA) to CD44 mols. Thus, anti-CD44 MoAb directed to HA-binding site could selectively inhibit CD3-mediated T cell activation. Furthermore, CD44-mediated inhibitory signals would be linked to the blocking of early CD3-mediated signal transduction.

RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 4

Full Text	Citing References
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AN 1998:114445 CAPLUS

DN 128:229087

TI Proteolytic enzymes modulate the adhesion molecule **CD44** on malignant cells in vitro

AU Gebauer, F.; Micheel, B.; Stauder, G.; Ransberger, K.; Kunze, R.

CS Imtox Inc., Berlin, D-13355, Germany

SO International Journal of Immunotherapy (1997), 13(3/4), 111-119
CODEN: IJIMET; ISSN: 0255-9625

PB Bioscience Ediprint Inc.

DT Journal

LA English

AB The adhesion mol. **CD44** and variants of the mol. on tumor cells are involved in the process of tumor progression and metastasis. The authors investigated the ability of several proteolytic enzymes to modulate the **CD44** mol. on different tumor cell lines. The authors found that proteolytic enzymes like bromelain, papain, and chymotrypsin were able to modulate **CD44** on cells of leukemic origin as well as on melanoma and mammary carcinoma cell lines. The authors could demonstrate that three different epitopes of **CD44** detected by the monoclonal antibodies L-178, J-173, and A3D8 were more or less reduced after enzymic treatment. The most pronounced effect was found using the plant protease bromelain. But protease treatment did not only reduce the concn. of **CD44** epitopes on the surface of tumor cells, the **CD44** also mediated adhesion as the authors were able to show for a cell line derived from a histiocytic lymphoma and for a melanoma cell line (U937 and SK-MEL28). These results imply that treatment with proteolytic enzymes might be useful in reducing the metastatic behavior of malignant cells. Finally, these data are discussed with regard to the potential role of therapeutically used enzymes in future cancer disease therapy.

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 10 OF 11 Elsevier BIOBASE COPYRIGHT 2006 Elsevier Science

Full Text	Citing References
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B.V. on STN
 AN 1995067606 ESBIODASE
 TI The effect of in vivo IL-7 deprivation on T cell maturation
 AU Bhatia S.K.; Tygrett L.T.; Grabstein K.H.; Waldschmidt T.J.
 CS Dr. T.J. Waldschmidt, Department of Pathology, Univ. of Iowa College of
 Medicine, Iowa City, IA 52242, United States.
 SO Journal of Experimental Medicine, (1995), 181/4 (1399-1409)
 CODEN: JEMEA V ISSN: 0022-1007
 DT Journal; Article
 CY United States
 LA English
 SL English
 AB A number of previous studies have suggested a key role for interleukin 7
 (IL-7) in the maturation of lymphocytes. To better assess the function
 of IL-7 in lymphopoiesis, we have deprived mice of IL-7 in vivo by
 long-term administration of a neutralizing anti-IL-7 antibody. In a
 previous report (Grabstein, K. H., T. J. Waldschmidt, F. D. Finkelman, B.
 W. Hess, A. R. Alpert, N. E. Boiani, A. E. Namen, and P. J. Morrissey.
 1993. J. Exp. Med. **178**:257-264), we used this system to demonstrate the
 critical role of IL-7 in B cell maturation. After a brief period of
 anti-IL-7 treatment, most of the pro-B cells and all of the pre-B and
 immature B cells were depleted from the bone marrow. In the present
 report, we have injected anti-IL-7 antibody for periods of up to 12 wk to
 determine the effect of in vivo IL-7 deprivation on the thymus. The
 results demonstrate a >99% reduction in thymic cellularity after extended
 periods of antibody administration. Examination of thymic CD4- and CD8-
 defined subsets revealed that, on a proportional basis, the CD4+, CD8+
 subset was most depleted, the CD4 and CD8 single positive cells remained
 essentially unchanged, and the CD4-, CD8- compartment actually increased
 to .apprx.50% of the thymus. Further examination of the double negative
 thymocytes demonstrated that IL-7 deprivation did, indeed, deplete the
 CD3-, CD4-, CD8- precursors, with expansion of this subset being
 interrupted at the **CD44+**, CD25+ stage. The proportional increase in the
 CD4-, CD8- compartment was found to be due to an accumulation of CD3+, T
 cell receptor α, β + double negative T cells. Additional
 analysis revealed that anti-IL-7 treatment suppressed the
 audition/selection process of T cells, as shown by a significant
 reduction of single positive cells expressing CD69 and heat stable
 antigen. Finally, the effects of IL-7 deprivation on the thymus were
 found to be reversible, with a normal pattern of thymic subsets returning
 4 wk after cessation of treatment. The present results thus indicate a
 central role for IL-7 in the maturation of thymic-derived T cells.

L2 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

Full Text	Citing References
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AN 1994:525227 CAPLUS
 DN 121:125227
 TI Use of bromelain in cancer and metastasis treatment
 IN Ransberger, Karl
 PA Mucos Pharma GmbH und Co., Germany
 SO Ger. Offen., 11 pp.
 CODEN: GWXXBX
 DT Patent
 LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	DE 4302060	A1	19940728	DE 1993-4302060	19930126
PRAI	DE 1993-4302060		19930126		

AB Bromelain reduces the metastatic potential of cancer cells by structurally altering epitopes on the **CD44** surface glycoprotein responsible for metastasis. Its effect is enhanced by addn. of papain, trypsin, lipase, amylase, chymotrypsin, pancreatin, Serratia peptidase, and/or rutoside. Thus, incubation with bromelain or papain inhibited the reactivity of MOLT 4/8 leukemic T-cells with monoclonal antibodies to epitopes L-**178** and J-173 of **CD44**. This effect of bromelain was not abolished by α 2-macroglobulin.

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